

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re:	Rafael Storz	Confirmation No:	2551
Application No:	10/822,428	Art Unit:	1631
Filed:	April 12, 2004	Examiner:	Lin, Jerry
For:	Method for Separating Detection Channels of a Microscope System		
Customer No.:	29127		
Attorney Docket No.	21295.79 (H5786US)		

### **APPEAL BRIEF**

Mail Stop Appeal Brief—Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Applicants file this Appeal Brief following the October 29, 2008, filing of Notice of Appeal to the Board of Patent Appeals and Interferences from the final Office Action, mailed April 29, 2008, (Paper No. 20080417), and the Advisory Action, mailed July 29, 2008, (Paper No. 20080723).

A three-month extension is requested for this response.

**Real Party in Interest**

Leica Microsystems CMS GMBH, the assignee of the present application, is the  
real party in interest.

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**Related Appeals and Interferences**

None

**Status of Claims**

Claims 1, 2, and 5-16 are pending in this application. Claims 3-4 and 17 are cancelled. Claims 1, 2, and 5-16 are rejected. The rejection of claims 1, 2, and 5-16 is being hereby appealed.

### **Status of Amendments**

The proposed Amendment filed on June 27, 2008, after the Final Rejection had been denied entry.

**Summary of Claimed Subject Matter**

Claim 1 defines a method for separating detection channels, comprising the steps of:

providing a sample with at least two fluorescent dyes (15 in Fig. 2);

exciting the at least two fluorescent dyes with light of different excitation wavelengths, wherein the number of different excitation wavelengths does not exceed the number of fluorescent dyes in the sample (Specification paragraphs [0034]-[0036], Figs. 6-8);

obtaining a measured emission spectrum of the sample (Specification paragraphs [0034]-[0036], Figs. 6-8);

determining wavelength separation points of the emission spectrum (Specification paragraphs [0040]-[0041]) to allocate a corresponding portion of the measured emission spectrum to a corresponding detection channel (for example, 35, 36, 37 in Fig. 2); and

conveying light from the sample (15 in Fig. 2) into the different detection channels (for example, 35, 36, 37 in Fig. 2) according to the separation points (Specification paragraphs [0010] and [0029], Fig. 2),

wherein the separation points are determined by: finding a difference between an emission spectrum of one fluorescent dye of the at least two dyes present in the sample measured at a certain wavelength and a measured emission spectrum of the sample measured at the same wavelength (for example, 120, 121, 122 in Fig. 10); squaring the difference (for example, 123, 124, 125 in Fig. 11); and minimizing an integral of the square of the difference (Specification paragraphs [0040]-[0041], Figs. 10-11).

Claim 2 defines a method for separating detection channels, comprising the steps of:

providing a sample with at least two fluorescent dyes (15 in Fig. 2);  
exciting the at least two fluorescent dyes with light of different excitation wavelengths, wherein the number of different excitation wavelengths does not exceed the number of fluorescent dyes in the sample (Specification paragraphs [0034]-[0036], Figs. 6-8);

obtaining a measured emission spectrum of the sample (Specification paragraphs [0034]-[0036], Figs. 6-8);

determining wavelength separation points of the emission spectrum (Specification paragraphs [0040]-[0041]) to allocate a corresponding portion of the measured emission spectrum to a corresponding detection channel (for example, 35, 36, 37 in Fig. 2); and

conveying light from the sample (15 in Fig. 2) into the different detection channels (for example, 35, 36, 37 in Fig. 2) according to the separation points (Specification paragraphs [0010] and [0029], Fig. 2),

wherein the wavelength separation points of the portions of the emission spectrum are defined by intersection points of the individual spectra of each fluorescent dye in the sample (Specification paragraph [0037], Fig. 9).

Claim 5 is directed to the method as defined in Claim 1, wherein detection in the corresponding detection channel is performed with at least one detector element (Specification paragraphs [0013], [0028] and [0029], 19, 36, 37 in Figs. 1, 2).

Claim 6 is directed to the method as defined in Claim 5, wherein the detector element comprises several detector elements grouped together (Specification paragraph [0013]).

Claim 7 is directed to the method as defined in Claim 6, wherein signals of several detectors of a multi-anode photomultiplier are grouped together into one channel (Specification paragraphs [0013] and [0028]).

Claim 8 is directed to the method as defined in Claim 5, wherein the at least one detector element is a photomultiplier (Specification paragraphs [0013], [0028] and [0029], 36, 37 in Fig. 2).

Claim 9 is directed to the method as defined in Claim 1, wherein adjusting the separation between at least two channels is done by a selection means (Specification paragraphs [0014], [0028], Figs. 1, 2).

Claim 10 is directed to the method as defined in Claim 9, wherein the selection means is a micromirror array (Specification paragraphs [0014] and [0029]).

Claim 11 is directed to the method as defined in Claim 9, wherein the selection means is a spectral photometer (SP) module (Specification paragraphs [0014] and [0029], 20 in Fig. 2).

Claim 12 is directed to the method as defined in Claim 11, wherein the SP module comprises a mirror stop arrangement adjusted in such a way that each of the wavelength regions defined by the wavelength separation points is allocated, respectively, to one individual detection channel (Specification paragraphs [0014] and [0029], 34, 35 in Fig. 2).

Claim 13 is directed to the method as defined in Claim 1, wherein the wavelength separation points are determined by a computer system (Specification paragraphs [0028] and [0029], 23 in Figs. 1, 2).

Claim 14 is directed to the method as defined in Claim 13, wherein the data corresponding to the wavelength separation points are presented to a user on a display (Specification paragraphs [0028], [0029] and [0031], 27 in Figs. 2, 3).



Claim 15 is directed to the method as defined in Claim 14, wherein the user adjusts the mirror stop arrangement 34, 35 on the basis of the data presented on the display 27 (Specification paragraphs [0030] and [0031], Fig. 3).

Claim 16 is directed to the method as defined in Claim 13, further comprising automatically adjusting the mirror stop arrangement 34, 35 or the micromirror array is automatically adjusted in such a way that each wavelength region defined by the wavelength separation points is allocated to one its respective detection channel (Specification paragraph [0030], Fig. 3).

**Grounds of Rejection to be Reviewed on Appeal**

1. Whether Claims 1, 2, and 5-16 are unpatentable under 35 U.S.C. § 101.
2. Whether Claim 2 is unpatentable under 35 U.S.C. § 102(b) over Lybarger et al., *Dual-Color Flow Cytometric Detection of Fluorescent Proteins Using Single-Laser (488-nm) Excitation*, 31 Cytometry 147 (1998).

## **ARGUMENT**

### **Rejection under 35 U.S.C. § 101**

#### **Claims 1, 2, and 5-16**

The Court of Appeals for the Federal Circuit's recent *In re Bilski* decision clarified the bounds of patent-eligible subject matter for process claims. *See In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc). The *en banc Bilski* court held that "the machine-or-transformation test, properly applied, is the governing test for determining patent eligibility of a process under § 101." *Id.* at 956. The *Bilski* court further held that "the 'useful, concrete and tangible result' inquiry is inadequate [to determine whether a claim is patent-eligible under § 101.]" *Id.* at 959-60.

Examiner had been using this inadequate "useful, concrete and tangible result" inquiry to determine whether Claims are 35 U.S.C. § 101 patent-eligible and to reject Claims under 35 U.S.C. § 101, see, for example, the pending final Office Action, pages 2-3, and the pending Advisory Action, page 2.

Therefore, the Examiner's 35 U.S.C. § 101 rejection is defective and should be withdrawn.

The *Bilski* court, following Supreme Court precedent, enunciates the machine-or-transformation test as follows: "A claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." *Id.* at 954; *see also In re Comiskey*, 499 F.3d 1365, 1377 (Fed. Cir. 2007) (discussing the same test from *Diehr*, 450 U.S. 175).

Claims comprise exciting fluorescent dyes in a sample with light and conveying light from the sample into the different detection channels according to determined separation points.

The claimed processes are tied to a machine or apparatus capable of exciting fluorescent dyes in a sample with light.

The claimed processes are also tied to a machine or apparatus capable of conveying light from the sample into the different detection channels according to determined separation points.

The claimed processes comprise exciting the at least two fluorescent dyes in a sample; this transforms the sample into a different state.

The claimed processes comprise conveyance of light, i.e. of electromagnetic waves, via a channel; this transforms the state of electromagnetic field within the channel; and this transforms the channel into a different state.

Therefore, Applicants respectfully assert that Claims are 35 U.S.C. § 101 patent-eligible and that Claims should be allowed.

**Rejection under 35 U.S.C. § 102(b) over Lybarger et al., *Dual-Color Flow Cytometric Detection of Fluorescent Proteins Using Single-Laser (488-nm) Excitation*, 31 Cytometry 147 (1998)**

**Claim 2**

Unless a publication discloses within the four corners of the document not only all of the elements and limitations claimed but also all of the elements and limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102, *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (quoting *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)).

Claim 2 comprises the wavelength separation points of portions of the emission spectrum defined by intersection points of individual spectra of fluorescent dyes in a sample.

Examiner asserts in the pending final Office Action, pages 4-5, that “Lybarger et al. teach a method . . . wherein the separation points of the portions of emission spectrum are defined by the intersection points (page 149).” This is the entire discussion of this element of Claim 2 in the pending final Office Action.

The pending Advisory Action states the following on page 2 (typos corrected):

Applicants have responded to this rejection by stating Lybarger et al. do not describe separation points as defined by intersection of the spectra. The Examiner disagrees. On page 149, Lybarger et al. state that based on their spectral data (i.e. the wavelength separation points), “it may be possible to design optical filter combinations to monitor expression of

EGFP and EYFP independently.” On page 151, right column, Lybarger et al. disclose optical filter combinations that separate the emission spectrum based on their spectral data. Thus Lybarger et al. have taught determining wavelength separation points as well as conveying the light according to the separation points.

This is the entire discussion of the aforementioned element of Claim 2 in the pending Advisory Action.

In summary, the final Office Action states (without any further details) that Lybarger et al. disclose the aforementioned element of Claim 2 on page 149; while the Advisory Action does not even assert that Lybarger et al. disclose any use of intersections of spectra.

Neither the pending final Office Action nor the pending Advisory Action specify where on page 149 (or elsewhere) Lybarger et al. disclose separation points of portions of the emission spectrum defined by intersection of the spectra.

Applicants respectfully assert that, contrary to the present invention, Lybarger et al. do not disclose separation points defined by intersection of the spectra either on page 149 or anywhere else. Page 149 shows some intersecting spectra, but Lybarger et al. do mark or use the intersection points in any way on page 149 or anywhere else.

Therefore, Applicants respectfully assert that Claim 2 is 35 U.S.C. § 102 patent-eligible over Lybarger et al., *supra*, and that Claim 2 should be allowed.

For the foregoing reasons, Applicants believe that the pending rejections should be withdrawn, and that the present application should be passed to issue. Should any questions arise please contact the undersigned.

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Respectfully submitted,

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**Claims Appendix**

Claim 1 (previously presented): A method for separating detection channels, comprising the steps of:

- providing a sample with at least two fluorescent dyes;
- exciting the at least two fluorescent dyes with light of different excitation wavelengths, wherein the number of different excitation wavelengths does not exceed the number of fluorescent dyes in the sample;
- obtaining a measured emission spectrum of the sample;
- determining wavelength separation points of the emission spectrum to allocate a corresponding portion of the measured emission spectrum to a corresponding detection channel; and
- conveying light from the sample into the different detection channels according to the separation points,
- wherein the separation points are determined by:
  - finding a difference between an emission spectrum of one fluorescent dye of the at least two dyes present in the sample measured at a certain wavelength and a measured emission spectrum of the sample measured at the same wavelength;
  - squaring the difference; and
  - minimizing an integral of the square of the difference.

Claim 2 (previously presented): A method for separating detection channels, comprising the steps of:

- providing a sample with at least two fluorescent dyes;



exciting the at least two fluorescent dyes with light of different excitation wavelengths, wherein the number of different excitation wavelengths does not exceed the number of fluorescent dyes in the sample;

obtaining a measured emission spectrum of the sample;

determining wavelength separation points of the emission spectrum to allocate a corresponding portion of the measured emission spectrum to a corresponding detection channel; and

conveying light from the sample into the different detection channels according to the separation points,

wherein the wavelength separation points of the portions of the emission spectrum are defined by intersection points of the individual spectra of each fluorescent dye in the sample.

Claims 3-4 (canceled)

Claim 5 (previously presented): The method as defined in Claim 1, wherein detection in the corresponding detection channel is performed with at least one detector element.

Claim 6 (original): The method as defined in Claim 5, wherein the detector element comprises several detector elements grouped together.

Claim 7 (original): The method as defined in Claim 6, wherein signals of several detectors of a multi-anode photomultiplier are grouped together into one channel.

Claim 8 (original): The method as defined in Claim 5, wherein the at least one detector element is a photomultiplier.

Claim 9 (previously presented): The method as defined in Claim 1, wherein adjusting the separation between at least two channels is done by a selection means.

Claim 10 (original): The method as defined in Claim 9, wherein the selection means is a micromirror array.

Claim 11 (previously presented): The method as defined in Claim 9, wherein the selection means is a spectral photometer (SP) module.

Claim 12 (previously presented): The method as defined in Claim 11, wherein the SP module comprises a mirror stop arrangement adjusted in such a way that each of the wavelength regions defined by the wavelength separation points is allocated, respectively, to one individual detection channel.

Claim 13 (previously presented): The method as defined in Claim 1, wherein the wavelength separation points are determined by a computer system.

Claim 14 (previously presented): The method as defined in Claim 13, wherein the data corresponding to the wavelength separation points are presented to a user on a display.

Claim 15 (original): The method as defined in Claim 14, wherein the user adjusts the mirror stop arrangement on the basis of the data presented on the display.

Claim 16 (previously presented): The method as defined in Claim 13, further comprising automatically adjusting the mirror stop arrangement or the micromirror array is automatically adjusted in such a way that each wavelength region defined by the wavelength separation points is allocated to one its respective detection channel.

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Claim 17 (canceled)

**Evidence Appendix**

None

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**Related Proceedings Appendix**

None